Phenyloxazoline Derivatives of Amino-sugars. Part II.[1] The Fission of Phenyloxazolines under Basic Conditions

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Benzyl 2,3-dideoxy-5,6-*O*-isopropylidene-2'-phenyl-β-D-allofuranosido[2,3-*d*]-$\Delta^{2'}$-oxazoline (6) was hydrolysed to the corresponding benzamido-alcohol (10) on treatment with toluene-*p*-sulphonic acid in aqueous pyridine at 100°, conditions which did not hydrolyse the *O*-isopropylidene group. Compound (6) was degraded by potassium t-butoxide in dimethyl sulphoxide at 80° to a mixture of products including the enamide (12) and the benzamido-alcohol (10).

OXAZOLINES [2] are of considerable interest in many branches of chemistry including the carbohydrate field.[3] Although there are a few reports [4] on the hydrolysis of phenyloxazolines to amino-alcohols under alkaline conditions they are generally fairly stable to these conditions, *e.g.* the benzylation [5a] of the phenyloxazoline (2) with benzyl chloride and sodium hydroxide at 120° was accomplished in high yield. 2-Methyloxazolines are also hydrolysed by base [6a] and ethyl Δ^2-oxazoline-4-carboxylates are readily hydrolysed to formamido-alcohols by aqueous triethylamine.[6b]

Our usual route [1,7] to phenyloxazoline derivatives of

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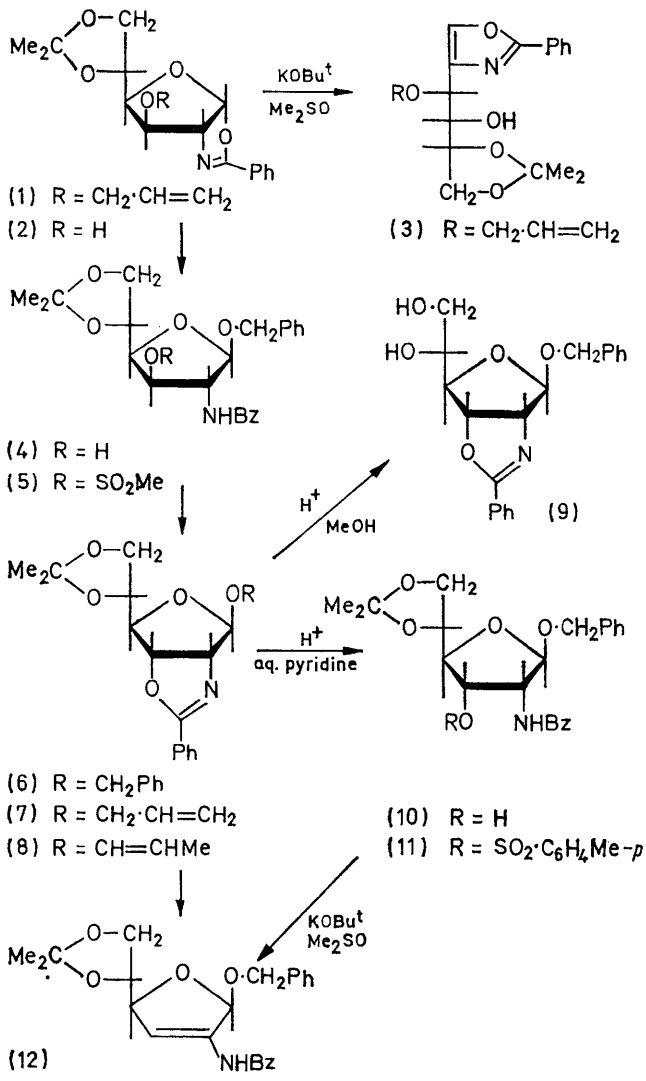
[4] K. Pfister, C. A. Robinson, A. C. Shabica, and M. Tishler, *J. Amer. Chem. Soc.*, 1949, **71**, 1101; C. W. Crane and H. N. Rydon, *J. Chem. Soc.*, 1947, 766.

[5] (*a*) R. Gigg and C. D. Warren, *J. Chem. Soc.* (*C*), 1968, 1903; (*b*) J. Gigg and R. Gigg, *ibid.*, 1966, 82.

[6] (*a*) R. Greenhalgh, R. M. Heggie, and M. A. Weinberger, *Canad. J. Chem.*, 1963, **41**, 1662; (*b*) D. Hoppe and U. Schöllkopf, *Angew. Chem. Internat. Edn.*, 1972, **11**, 432.

[7] R. Gigg and C. D. Warren, *J. Chem. Soc.*, 1965, 1351; *J. Chem. Soc.* (*C*), 1968, 2661.

amino-sugars involves heating solutions of vicinal benzamido-methanesulphonates in pyridine for several hours. However when a solution of the methanesulphonate (5) [1] in aqueous pyridine was heated, the



phenyloxazoline (6) [1] formed initially was converted into the benzamido-alcohol (10). Protonation of the oxazoline ring by the liberated methanesulphonic acid must therefore occur under these conditions, with subsequent attack by hydroxide ion and collapse of the intermediate 2-hydroxy-2-phenyloxazolidine [8] to give the benzamido-alcohol. Under these conditions the 5,6-*O*-isopropylidene group remained unhydrolysed, whereas in acidic methanol the 5,6-*O*-isopropylidene group of compound (6) was preferentially hydrolysed to give the phenyloxazoline (9).[1] When the phenyloxazoline (6) was treated with 2·5N-sodium hydroxide in aqueous ethanol it was slowly converted into an amine, which on benzoylation gave the benzamido-alcohol (10).

The phenyloxazoline (1) is rapidly degraded [5a] to the oxazole (3) by the action of potassium t-butoxide in dimethyl sulphoxide at room temperature, but the phenyloxazoline ring in compound (7) is only degraded at higher temperatures.[1] At 80° the phenyloxazoline (6) was converted into several products; one of the minor ones was the benzamido-alcohol (10). One of the major products gave a blue colour on t.l.c. plates after being sprayed with 50% sulphuric acid and kept at room temperature and also gave a purple colour with Ehrlich's reagent.[9] By analogy with the products obtained in the Morgan–Elson reaction,[10–12] it was considered that the major chromogenic product was the enamide (12). To confirm this structure, the toluene-*p*-sulphonate (11) was treated with potassium t-butoxide in dimethyl sulphoxide (conditions known [13] to be excellent for the elimination of sulphonate esters); an identical product, was obtained in high yield which had analytical data and an n.m.r. spectrum consistent with structure (12).

EXPERIMENTAL

Solvents were evaporated off under reduced pressure. Optical rotations were measured at 22—24° with a Bendix Automatic Polarimeter. T.l.c. was carried out with silica gel G. The light petroleum had b.p. 40—60° unless otherwise stated.

Benzyl 2-Benzamido-2-deoxy-5,6-O-isopropylidene-β-D-allofuranoside (10).—A solution of benzyl 2,3-dideoxy-5,6-*O*-isopropylidene-2′-phenyl-β-D-allofuranosido[2,3-*d*]-$\Delta^{2'}$-oxazoline (6) [1] (780 mg) in pyridine (20 ml) and water (5 ml) containing toluene-*p*-sulphonic acid monohydrate (300 mg) was kept at 100° for 24 h; t.l.c. (toluene–acetone, 9 : 1) then showed complete conversion of the starting material (R_F 0·75) into a new product (R_F 0·2). An excess of sodium hydrogen carbonate was added and the solvents were evaporated off. Toluene was evaporated from the residue to remove traces of pyridine and water and the product (750 mg) was then extracted with chloroform. The *benzamido-derivative* (10) (which gave gelatinous solutions when concentrated in ether or chloroform) was obtained as needles (from ether–light petroleum), m.p. 103—105°, $[\alpha]_D$ −25·9° (*c* 1 in $CHCl_3$) (Found: C, 66·9; H, 6·5; N, 3·5. $C_{23}H_{27}NO_6$ requires C, 66·8; H, 6·6; N, 3·4%), $\nu_{max.}$ 3400 (OH and NH), 1645, and 1520 cm^{-1} (CONH); acetate, m.p. 130—132°, $\nu_{max.}$ 3400 (NH), 1745 (OAc), 1650, and 1530 cm^{-1} (CONH). Hydrolysis in aqueous methanolic 0·5N-hydrochloric acid at reflux for 30 min gave 2-benzamido-2-deoxy-D-allose, m.p. and mixed m.p. 202—204° (decomp.) (from aqueous ethanol), $[\alpha]_D$ −26° (*c* 1 in Me_2SO, after 24 h) {lit.[1] m.p. 204° (decomp.), $[\alpha]_D$ −24° (*c* 1 in Me_2SO, after 24 h)}.

Benzyl 2-Benzamido-2-deoxy-5,6-O-isopropylidene-3-O-p-tolylsulphonyl-β-D-allofuranoside (11).—The benzamido-derivative (10) (2·7 g) and toluene-*p*-sulphonyl chloride (4 g) in dry pyridine (20 ml) were kept at 20° until t.l.c. (toluene–acetone, 6 : 1) showed complete conversion of the starting material (R_F 0·3) into the product (R_F 0·6). The mixture

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[11] R. Kuhn and G. Krüger, *Chem. Ber.*, 1956, **89**, 1473; 1957, **90**, 264.
[12] D. H. Leaback and P. G. Walker, *Biochim. Biophys. Acta*, 1963, **74**, 297.
[13] C. H. Snyder and A. R. Soto, *J. Org. Chem.*, 1964, **29**, 742.

was poured into water and the product was filtered off to give the *toluene*-p-*sulphonate* (11) (2·4 g), m.p. 96—99° (from aqueous ethanol), $[\alpha]_D$ −40° (*c* 1 in $CHCl_3$) (Found: C, 62·95; H, 5·7; N, 2·8; S, 5·45. $C_{30}H_{33}NO_8S$ requires C, 63·5; H, 5·9; N, 2·5; S, 5·6%).

Benzyl 2-*Benzamido*-2,3-*dideoxy*-5,6-O-*isopropylidene*-β-D-erythro-*hex*-2-*enofuranoside* (12).—A solution of the toluene-*p*-sulphonate (11) (2 g) in dry dimethyl sulphoxide (50 ml) containing potassium t-butoxide (1 g) was stirred at 70° for 15 min; t.l.c. (chloroform–ethyl acetate, 3 : 1) then showed complete conversion of the starting material (R_F 0·8) into a major product (R_F 0·75) and a minor product (R_F 0·4). The former gave a blue colour on t.l.c. plates after being sprayed with 50% sulphuric acid and kept at room temperature, and a purple colour with Ehrlich's reagent [9] at room temperature. The mixture was diluted with water and the product extracted with ether and chromatographed on alumina. Elution with ether gave the *unsaturated glycoside* (12) (600 mg) as a thick syrup, $[\alpha]_D$ −28° (*c* 1 in $CHCl_3$) (Found: C, 69·8; H, 6·3; N, 3·6. $C_{23}H_{25}NO_5$ requires C, 69·85; H, 6·4; N, 3·5%), $\nu_{max.}$ 3300 (NH), 1660, and 1540 cm^{-1} (CONH), τ 1·98 (s, NH which had almost disappeared 3 h after the addition of D_2O), 2·20—2·37 (2H, m, benzamide *ortho*-protons), 2·57—2·67 (8H, m, benzamide *meta*- and *para*-protons and $C_6H_5{\cdot}CH_2$), 3·40 (1H, unresolved m, H-3), 5·3 (3H, q and broad s, $PhCH_2$ and H-4), 6·02 (3H, unresolved m, H-5, H-6, and H-6′), and 8·58 (s) and 8·70 (s) (6H, CMe_2).

Action of Potassium t-Butoxide in Dimethyl Sulphoxide on the Phenyloxazoline (6).—Potassium t-butoxide (2 g) was added to a solution of the phenyloxazoline (6) (2 g) in dry dimethyl sulphoxide (20 ml); the solution was stirred at 80° for 1 h. T.l.c. (toluene–acetone, 6 : 1) then showed complete conversion of the starting material (R_F 0·6) into two major products (R_F 0·46 and 0·36) and three minor products (R_F 0·64, 0·22, and 0·16). The products of R_F 0·46 and 0·16 gave a blue colour on the t.l.c. plates when sprayed with 50% sulphuric acid and kept at room temperature, and also gave a purple colour with Ehrlich's reagent. The mixture was diluted with water and the products extracted with chloroform. After drying (Na_2SO_4) and evaporation of the solvent the syrupy product was chromatographed on alumina. Elution with ether–light petroleum (2 : 1) gave the minor product (R_F 0·64) (190 mg); elution with ether gave the major product (R_F 0·46) (520 mg) and then a mixture of the two major products (R_F 0·46 and 0·36) (400 mg). The product of R_F 0·46 was identical (i.r. spectrum and t.l.c.) with compound (12) prepared as already described. The slower running products (R_F 0·22 and 0·16) were isolated in a separate experiment by chromatography on silica gel and crystallisation from ether–light petroleum. The product of R_F 0·22, m.p. and mixed m.p. 103—105°, was identical (t.l.c. and i.r. spectrum) with benzyl 2-benzamido-2-deoxy-5,6-*O*-isopropylidene-β-D-allofuranoside (Found: C, 66·5; H, 6·2; N, 3·6%).

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